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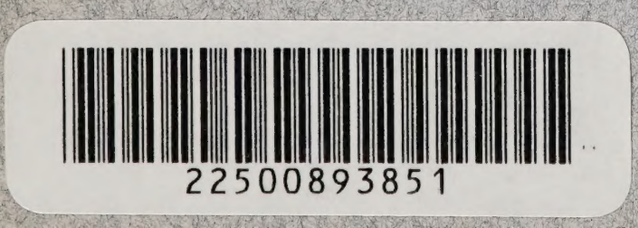

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THE RELATION OF TONUS TO ANTIPERISTALSIS IN THE COLON.

By W. B. CANNON.

[*From the Laboratory of Physiology in the Harvard Medical School.*]

IN Jacobi's incidental mention of antiperistalsis on the cat's colon, he noted that the waves started from a more or less broad constriction ring.[1] In the report of my observations on colonic antiperistalsis, made without knowledge of Jacobi's record, I stated that the waves began "at the nearest tonic constriction."[2] Elliott and Barclay-Smith also observed in various instances that the waves, both in the cat and the rat, were initiated "at the anal limit of a distended area," "from the upper limits of a ring of constriction," "from a deep constriction which formed and remained with slight oscillations as a starting point."[3] Fig. 6 in my paper and Figs. 2 and 3 in the paper by Elliott and Barclay-Smith represent clearly the waves passing away from the tonic ring[4] of origin. Although we thus reported our observations, none of us seems to have realized adequately the significance of the ring of tonic constriction as the source of antiperistalsis.

Two years ago I reported that by producing a tonic ring in the proximal colon exposed under warm normal salt solution, either by pinching the gut or by applying with a brush a weak solution of barium

[1] JACOBI: Archiv für experimentelle Päthologie und Pharmakologie, 1890, xxvii, p. 147.

[2] CANNON: This journal, 1902, vi, p. 265.

[3] ELLIOTT and BARCLAY-SMITH: Journal of physiology, 1904, xxxi, pp. 280, 281, 284–285.

[4] The tonic state is conceived in this and the following paper as a persistent shortened condition of the musculature without any theory as to its being due to continued excitation. (See BIEDERMANN, Archiv für die gesammte Physiologie, 1904, cii, p. 520.) The tonic ring is a region in which the persistent shortening is greater than elsewhere.

chloride, waves could be made to appear at will. By making the ring at the cæcum, repeated downward-running waves may be set going; by making a new ring now at the terminus of these waves, reversed waves appear and meet the downward waves progressively nearer the cæcum until only reversed waves are running; furthermore, a tonic ring made midway in the proximal colon has been seen giving rise to repeated waves which passed away in both directions.[5] These activities have been observed not only in the colon still receiving its normal blood supply, but also in the excised colon, tied full of fluid, and kept alive in warm oxygenated Ringer's solution. The waves have also been seen passing away from a tonic ring in the excised colon of the rabbit. The phenomena of the tonic ring are therefore of prime importance in explaining the occurrence of both peristalsis and antiperistalsis of the large intestine. In this paper I propose to examine further these phenomena, as well as some characteristics of the antiperistaltic waves, in an attempt to find the more intimate relations between these two activities of the gut.

FIGURE 1. — Photograph of the colon of the cat, exposed under warm normal salt solution. A series of antiperistaltic waves are shown passing away from the tonus ring, which is marked by an arrow.

CHARACTERISTICS OF COLONIC ANTIPERISTALSIS.

The first characteristic of colonic antiperistalsis, which distinguishes it from peristalsis of the small intestine, is the absence of a region of inhibition projected before any moving constriction. As a result the constrictions continue passing over the proximal colon in a close series (Fig. 1), each succeeding ring never checking or interfering in any way with those already started and progressing before it.

The antiperistaltic waves, which run thus in a series, appear rhythmically. They must therefore start at a source that is rhythmically

[5] CANNON: This journal, 1909, xxiii, p. xxvii.

active. If an animal is etherized, its spinal cord destroyed below the brachial region, and the abdomen opened under warm salt solution, the colon can be directly watched. If the colon is inactive, but not wholly relaxed, it can be made to exhibit peristalsis by producing a tonic ring with barium chloride. The ring first contracts strongly; then, as it slightly relaxes, it can be seen pulsating rhythmically. Inspection of the colon under these circumstances shows that each pulsation sends away a moving constriction — a wave of peristalsis. The same phenomenon is observed when the colon is spontaneously active. The rhythmically beating tonic ring is therefore the source of the rhythmically recurring waves.

The Importance of Internal Pressure.

Antiperistalsis in the colon is dependent on a state of tension. The evidence for this statement is as follows. If a tube is tied into the colon and, as fluid is introduced, a tonic ring is made, antiperistaltic waves are usually started by the ring. If now the fluid is largely withdrawn, visible waves cease. Reintroducing the fluid starts them again. The observation which I made in 1901, that antiperistalsis begins whenever new material is pushed into the colon from the ileum, and Elliott and Barclay-Smith's method of starting the waves by injecting air or gruel, agree completely with other evidence that distention of the gut is the condition under which the waves originate. Indeed, Elliott and Barclay-Smith ascribe the appearance of the waves to distention.[6]

Mechanical extension is well recognized as a most efficient stimulus for exciting activity in smooth muscle. Sokoloff and Luchsinger, who observed the activity of the excised ureter through which normal salt solution was forced under varying pressures, reported that within wide limits the higher the pressure, the more frequent the pulsations, and expressed the view that a certain tension was the condition for the appearance of spontaneous contractions.[7] Guyon has reported similarly the contraction of the bladder as the result of distention to

[6] Elliott and Barclay-Smith: *Loc. cit.*, p. 278.

[7] Sokoloff and Luchsinger: Archiv für die gesammte Physiologie, 1881, xxvi, p. 467.

a requisite degree.[8] The manner in which the tonic neuromusculature of the excised stomach, which has been digesting, responds by contracting when distended by air has also been recorded.[9] Bayliss and Starling's observation that rhythmic contractions of the inactive small intestine of the cat appear when a balloon is inserted and inflated is further evidence for the same conclusion.[10] Of course, the attachment of a lever to a strip of smooth muscle (intestine, uterus) places the muscle in tension, and under the circumstances rhythmic contractions result and are readily recorded. Although strips of neuromusculature from the gut can contract spontaneously while resting without obvious tension in Ringer's solution,[11] yet the observations above cited point clearly to the importance of stretching as a highly efficient agency for evoking contractile response in smooth muscle.[12] Since smooth muscle surrounds hollow organs, which gradually fill and must be emptied, the value of distention as a stimulus is obvious.

The Importance of the Tonic State.

The extension of smooth muscle which evokes a contractile response must not, however, be merely the elongation of non-elastic substance. When smooth muscle is flaccid and toneless, extension calls forth no response. Only when the muscle is shortened and resilient, *i. e.*, in a state of tonus, does a pull result in a contraction. Thus the vagus nerves supply tonic impulses to the œsophagus and stomach. Immediately after the vagi are severed food gathers in the toneless œsophagus without causing any contractile reaction of the smooth muscle in the wall. Only after time has elapsed and a tonic state of the neuromusculature has been developed intrinsically, does the presence of food in the lower œsophagus again cause contraction.[13] Similarly impaired action of the rectum, the stomach, and the bladder has been observed immediately after severance of the nerves which

[8] Guyon: Comptes rendus de la Société de Biologie, 1900, lii, p. 712.

[9] Cannon: This journal, 1907, xx, p. 301.

[10] Bayliss and Starling: Journal of physiology, 1901, xxvi, p. 134.

[11] See Magnus: Archiv für die gesammte Physiologie, 1906, cxi, p. 153.

[12] The same conclusion has been drawn with reference to the cardiac muscle of invertebrates (see Carlson: This journal, 1905, xii, p. 488).

[13] Cannon: This journal, 1907, xix, p. 443.

supply tonic influences to these organs.[14] Yet all these organs are capable of action when isolated from the central nervous system, but only after recovery of a tonic state. The tonic state is fundamental. I have repeatedly attempted to call forth rhythmic contractions, both in the atonic colon and in the atonic stomach, by distention, but without success. The tonic state is therefore quite as important as the internal pressure, — indeed, it is the condition for the existence of that pressure.

According to Schultz,[15] smooth muscle when in a short state is extended more readily by a moderate load than when in a long state and weighted with the same load. As Figs. 1 and 4 show, the tonic ring is a region contracted more than the neighboring regions, and ring *b* (Fig. 4), which is the pulsatile source of waves, is more contracted than ring *a*, which under the same pressure has ceased to pulsate (see p. 246). On the basis of Schultz's evidence we may assume, therefore, that at the tonic ring the neuromusculature may be in a condition especially favorable to distention by pressure. Furthermore, as already stated, since the ring is in tonic contraction, it will respond to extension by contraction.

The Rôle of the Refractory Period.

Magnus has brought forward evidence that during the period of shortening and the first part of the period of relaxation, the neuromusculature of the small intestine is relatively refractory both to electrical and to mechanical stimulation,[16] and that it only gradually, during relaxation, recovers full irritability. The neuromusculature of the stomach likewise, according to Ducceschi, passes through these same phases.[17] Refractoriness does not imply necessarily total abolition of excitability, it may mean only much diminished excitability

[14] Elliott and Barclay-Smith: Journal of physiology, 1904, xxxi, p. 289; Cannon: This journal, 1906, xvii, p. 441; Elliott: Journal of physiology, 1907, xxxv, pp. 424, 425.

[15] Schultz: Archiv für Physiologie, 1903, Supplement-Band, p. 25.

[16] Magnus: Archiv für die gesammte Physiologie, 1904, ciii, p. 540; 1906, cxi, p. 152.

[17] Ducceschi: Archivio per le scienze mediche, 1897, xxi, p. 170.

as is the case during systole of the invertebrate heart.[18] As Fig. 2 shows, the neuromusculature of the colon is also refractory to stimulation while shortening, — either pinching close to the contracting ring, or pulling the ring sharply by traction on the lever, has no effect at this stage, although similar stimulation while the muscle is relaxing causes contraction. When the tonic ring begins to contract, therefore, in response to distention, it becomes refractory to the stimulus, *i. e.*, to the internal pressure. It begins again to be subject to this stimulus after having reached its most contracted state and partly relaxed, — *i. e.*, when again readily distensible. Now, on being distended by the internal pressure, the ring is stimulated, and as before responds in contraction. Thus, by the existence of the tonic state, by the presence of internal pressure, by the response of the tonic neuromusculature to the mechanical extension, and by its refractoriness during the period of shortening, the pulsations of the tonic ring can be accounted for.

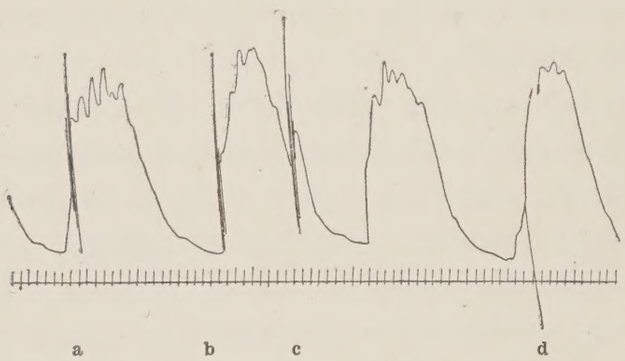

FIGURE 2. — Record showing the refractoriness of the large intestine to mechanical stimulation while contracting, and its irritability while relaxing. At *a*, *b*, *c* the stimulus was repeated pinching; at *d*, quick stretching.

THE TRANSMISSION OF THE ANTIPERISTALTIC WAVES.

The movement of a wave of constriction away from the pulsating tonic ring must now be regarded. In simple neuromuscular structures, especially in the functioning of the nerve net of invertebrates, v. Uexküll has so frequently observed that the state of excitation moves from an active to a less active region that he has declared the general law — "in a nerve net excitation flows from a place of higher tonus to a place of lower tonus," "from a contracted to a stretched muscle."[19] The departure of waves from a pulsating ring backwards, or forwards, or in both directions simultaneously, as described above, can thus be

[18] See CARLSON: This journal, 1906, xvi, p. 82.

[19] v. UEXKÜLL: Ergebnisse der Physiologie, 1904, iii [2], p. 4.

explained. It is not clear, however, that the spreading of the state of excitation into a freshly distended area, merely as a wave of internal change, is the manner by which the constrictions move. It is possible to invoke again in this progression of the constrictions the factors to which have been ascribed the pulsations of the tonic ring. Evidently any contraction of the tonic ring must increase internal pressure on neighboring parts of the intestinal wall. The muscles in these regions therefore are set in greater tension. As a result of the extra stretching, the muscle rings begin to contract and thus to distend the regions beyond, which in turn are stimulated. Thus, as a result of spreading distention, the passage of the constriction from the pulsating ring to inactive areas of the gut might be explained.

In this connection may be considered the reasons for the tonic ring normally sending away waves in only one direction, — *i. e.*, giving rise only to *antiperistalsis*. All instances of *peristalsis* have appeared, in my experience, when the colon has been injected with fluid to such an extent that a fluid content is present distal to the pulsating ring. Thus, when the waves pass away in both directions from the ring, the fluid character of the contents is the same in both directions. Under normal conditions, however, such is not the case. The contents become remarkably more viscous as they accumulate in the mid-region of the colon, indeed they may change to hard nodules. A tonic ring, with a fluid content on one side and a viscous mass on the other, would have different effects distally and proximally as it pulsated; through the viscous content it could not readily distend the wall and would therefore fail to discharge a wave distally; through the fluid content it would have its usual effect. Of course, if the distal content were moved by the contraction of the ring, the result would in all probability be different, for in that case there would be a moving stimulus. The observation of Elliott and Barclay-Smith — that in the rat the proximal colon, which is commonly worked over by antiperistaltic waves if the material it receives is soft and moist, exhibits the peristaltic reflex if the material is stiff and dry [20] — points clearly to the importance of consistency of the contents in determining the appearance of antiperistalsis.

A corollary from the foregoing discussion is that the less contracted region must itself still be in a condition to undergo distention, — it

[20] Elliott and Barclay-Smith: *Loc. cit.*, p. 285.

must, although not contracted, possess some degree of tonus in order to be in a state to respond to the extra pressure from within. If the gut is atonic and quite relaxed, the arousing of antiperistaltic waves from a pulsating ring is usually impossible. In my experience, also, waves do not move away from the ring if the gut expands sharply at the edge of the ring. Fig. 2 in Elliott and Barclay-Smith's paper [21] shows waves passing from a tonic ring to a region in less tonic contraction, but failing to pass to a region of full distention. In this case the distended and the contracted regions were separated by a rather abrupt change in the size of the lumen. The tube must taper from the less contracted part to the pulsating tonic ring or the pulsations of the ring will fail to discharge to the tube the moving constrictions.

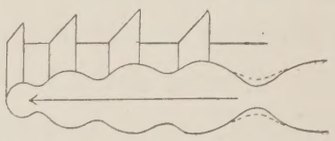

FIGURE 3. — Diagram of colonic antiperistalsis illustrating the regions refractory to stimulation (covered by horizontal lines), and irritable regions (covered by slanting lines). The rise of the slant lines indicates increase of irritability accompanying relaxation.

From the evidence that a refractory state attends the contractile period and that irritability is only gradually recovered during relaxation, the inferences are justified that the peristaltic contraction is itself a moving refractory phase of the neuromusculature, and that as it progresses it trails behind it a less irritable region. The condition that results in the colon is illustrated in the accompanying diagram of colonic antiperistalsis (Fig. 3). The narrowing at the right represents the pulsating tonic constriction, now contracted; the other narrowings represent waves moving away from the pulsating source. The horizontal lines extend in each instance, from left to right, over fibres just beginning to contract, fibres maximally contracted and fibres about one-third relaxed. The lines therefore lie above the parts of the muscular wall that are relatively refractory to stimulation. The slanted lines extend, left to right, from fibres about one-third relaxed to fibres wholly relaxed, — they reach, therefore, over regions in which irritability is being recovered. The upward slant of the lines indicates increasing susceptibility to stimulation as relaxation proceeds. Evidently the circumference fully relaxed is the region most ready to contract. This circumference in each instance is separated from the departing contracted region (that to the left in the diagram)

[21] ELLIOTT and BARCLAY-SMITH: *Loc. cit.*, p. 280.

by an area of diminished irritability. On the other hand, the most relaxed circumference is in each instance contiguous with the oncoming region of contraction. Thus, for example, if the circumference next the tonic ring has relaxed (as in Fig. 3), it is again most susceptible to an impulse coming to it from the pulsating source, or to increased pressure due to the pulsation. What is true of this relaxed circumference is true of each other fully relaxed band lying beyond — each is maximally irritable and most subject to the spread into it of the contraction phase existent on the side towards the tonic ring. Each is protected from being invaded by the contraction phase on the side away from the tonic ring by the intervening region of lessened irritability. Thus, if a contraction spreads, it necessarily spreads progressively from its origin into regions most ready to undergo contraction. And just as in the heart the pulsations of the sinus set the pace for contraction of the rest of the organ, so in the colon the pulsations of the ring determine the rate at which the waves shall appear.

FIGURE 4. — Photograph showing the blocking of antiperistaltic waves started at tonic ring *b*, by the nearly relaxed ring *a*.

The observation previously noted (see p. 239) that waves from a new tonic ring will sweep away opposing waves from an older ring indicate that the pulsations are more rapid in a state of high tonus than they are later when the tonic state has somewhat diminished, and that the new ring therefore sets a faster pace than the older. This inference is justified by the decrease in the rate of pulsation with decrease in tonus. In one instance, as the ring was relaxing, the rate decreased, within five minutes, from 6 to 5 waves per minute.

A tonic constriction is itself refractory to the stimulus that comes to it in the form of a moving constriction. This fact was noted by Bayliss and Starling in the small intestine;[22] — my observations and

[22] BAYLISS and STARLING: Journal of physiology, 1899, xxiv, p. 106.

those of Elliott and Barclay-Smith on the occurrence of antiperistaltic waves between the natural tonic constrictions of the distal colon also illustrate the definite boundaries set by the tonic state. The blocking of the waves started at tonic ring *b*, by the nearly relaxed ring *a* (Fig. 4), illustrates the refractoriness of the region in stronger tonus to influences from regions in weaker tonus.

The Relations of Tonus, Internal Pressure, and Peristalsis.

The dependence of pulsations on an adjustment between locally increased tonus and the internal pressure is also illustrated in Fig. 4. The colon was filled with fluid; ring *b*, which was deep, was pulsating and sending forth waves; ring *a*, which had partially relaxed, no longer pulsated. The two rings were exposed to approximately the same internal pressure; this was an adequate stimulus for the deeper ring, but not for the less deep. Under such circumstances I have been able to renew rhythmic activity in the quiet ring merely by increasing the internal pressure. In all probability this is what occurs when new food enters the large intestine from the ileum and starts a fresh series of antiperistaltic waves. The new food distends the walls. A general contraction of the proximal colon follows, which presses the food towards the region of the tonic rings.[23] The inactive nearest ring then begins to pulsate in response to the increased internal pressure and thus to send waves backward towards the cæcum. Once started the waves can be artificially augmented by increase of internal pressure; thus shallow constrictions can be made much deeper by a series of slight momentary pressures on the gut, which cause repeated slight distentions of the wall where the waves are passing — an effect similar to that observed by Ducceschi, that up to a certain degree distention increases the contractions of the stomach.[24]

The precise relation between the degree of tonus and the internal pressure which results in effective rhythmic contraction is difficult to define. When a tonic ring is first made, either by pinching or by applying barium chloride, it is a deep and strong contraction. Only when it has to some extent relaxed does the normal rhythm appear

[23] Cannon: This journal, 1902, vi, p. 268.

[24] Ducceschi: *Loc. cit.*, pp. 146, 149.

and begin to send off waves.[25] Also, as already noted, withdrawal of fluid contents from an active colon causes immediate cessation of activity, which returns only as the contents are reintroduced. On the other hand, if the internal pressure is sufficiently increased, the waves moving along the gut will disappear, and can be seen again only when the distention is lessened. Sokoloff and Luchsinger report a similar experience in their experiments on distention of the ureter,[26] and likewise Jastreboff in his observations on the contractions of the rabbit's vagina.[27] Both the tonus and the distending force, therefore, can be too great for effective rhythmic action.

The Origin of the Tonic Rings.

From the foregoing evidence and discussion we can understand that, given in the colon the state of tonus and a locally increased tonic contraction, augmentation of internal pressure can explain the appearance of colonic antiperistalsis. The conditions for the establishment of the tonic rings, however, are still undetermined. It is probably significant that the tonic rings are not formed in the proximal colon, but only some distance from the cæcum. Elliott and Barclay-Smith were unable to demonstrate any motor innervation of the proximal colon. Possibly the tonic rings are formed only in that part of the colon which receives a motor nerve supply, and that the tonic state of that region stimulates the parts nearer the cæcum. This suggestion is supported by the observation that when the motor nerves of the distal colon are severed, the antiperistaltic waves become after a time very feeble.[28] Since, however, the rings do persist for a while after destruction of the spinal cord, they can be maintained by the gut itself. Henderson has called attention to the importance of the normal content of carbon dioxide in the blood for the preservation of the tone of intestinal smooth muscle; and by retaining the normal

[25] At times, when the colon tapers towards the tonic ring, the region next the deepest tonus, somewhat less contracted, begins to pulsate before the ring pulsates. The tonus of this intermediate region can be regarded as adapted to the internal pressure. Compare the stomach (Cannon: This journal, 1911, xxix, p. 254).

[26] Sokoloff and Luchsinger: *Loc. cit.*, p. 466.

[27] Jastreboff: Archiv für Physiologie, 1884, p. 103.

[28] Elliott and Barclay-Smith: *Loc. cit.*, p. 287.

amount or by increasing it he has been able to induce antiperistalsis in the colon, as well as other movements of the canal.[29] That the proximal colon is the seat of the active fermentation which occurs in the large gut suggests the possibility that the tonic state may be in part at least due to the presence of intestinal gases.

Summary.

Antiperistaltic waves of the colon normally start at a tonic constriction in the gut, and they can be produced by making a tonic ring. They recur rhythmically, and originate in the rhythmic pulsations of the tonic ring.

These rhythmic pulsations are a response to the stretching of the tonically contracted muscle by internal pressure. Withdrawal of the colonic contents stops the pulsations, return of the contents restores them. If the muscle is not tonically contracted, internal pressure does not produce pulsations.

The tonic ring is especially subject to stimulation by distention. As the ring relaxes it pulsates less rapidly, and as it relaxes more it stops pulsating. Refractoriness to stimulation during contraction and the first part of relaxation explains the rhythmic response.

The waves pass away from the pulsating source probably as a result of stretching the relaxing muscular rings by increased internal pressure. As these waves are themselves moving refractory phases trailing regions of lessened irritability, they can only progress in a direction leading away from their source.

The precise relations between the state of tonus and the internal pressure which induce rhythmic response cannot yet be defined. The distending force, and the tonus also, may be too great or too slight to result in effective pulsations.

The conditions which originate the tonic state in the proximal colon are not yet definitely determined.

[29] Henderson, Y.: This journal, 1909, xxiv, p. 70.

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